

Complete Summary

GUIDELINE TITLE

Clinical guidelines for the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care.

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Primary Care. Clinical guidelines for the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care. London (UK): National Institute for Clinical Excellence (NICE); 2004 May. 311 p. [309 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
 METHODOLOGY - including Rating Scheme and Cost Analysis
 RECOMMENDATIONS
 EVIDENCE SUPPORTING THE RECOMMENDATIONS
 BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
 QUALIFYING STATEMENTS
 IMPLEMENTATION OF THE GUIDELINE
 INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT
 CATEGORIES
 IDENTIFYING INFORMATION AND AVAILABILITY
 DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Familial breast cancer

GUIDELINE CATEGORY

Counseling
 Evaluation
 Management
 Prevention
 Risk Assessment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Medical Genetics
Obstetrics and Gynecology
Oncology
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Nurses
Patients
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide recommendations for the classification and care of women at the risk of familial breast cancer in primary, secondary, and tertiary care

TARGET POPULATION

Women 18 years and older seen in primary, secondary, and tertiary care settings who are at risk of familial breast cancer

Note: This guideline does not cover the following populations:

- Women younger than 18 years of age
- Women who have breast cancer
- Men who may be at risk of familial breast cancer (although the recommendations will be pertinent)

INTERVENTIONS AND PRACTICES CONSIDERED

Care of all Women with a Family History of Breast Cancer

1. Counseling regarding risk factors identification and lifestyle modification related to:
 - Use of hormone replacement therapy (HRT)
 - Use of oral contraceptive
 - Breastfeeding
 - Alcohol consumption
 - Smoking
 - Weight maintenance
 - Physical activity
 - Menstrual/reproductive factors

Care of Women in Primary Care

1. First- and second-degree family history

2. Primary care management or referral, if applicable
3. Risk assessment
4. Provide patient education and support mechanisms (risk counseling, psychological counseling, risk management advice)

Care of Women in Secondary Care

1. Multi-disciplinary care planning
2. Family history, including third-degree family history
3. Risk assessment
4. Referral back to primary care, if applicable
5. Mammographic surveillance, when applicable
6. Provide support mechanisms (risk counseling, psychological counseling, risk management advice)
7. Magnetic resonance imaging (MRI) and ultrasound as indicated for follow-up of mammographic abnormalities
8. Referral to tertiary care, if applicable

Care of Women in Tertiary Care

1. Multi-disciplinary team planning
2. Clinical genetic risk assessment
3. Third-degree family history
4. Risk assessment and communication
5. Genetic counseling
6. Genetic testing (predictive and mutation finding)
7. Risk-reducing surgery
 - Bilateral mastectomy
 - Bilateral oophorectomy

Note: Guideline developers discussed but did not recommend tamoxifen as chemoprophylaxis in women who do not have breast cancer.

MAJOR OUTCOMES CONSIDERED

- Levels and estimates of risk of breast cancer
- Rates of detection of breast cancer
- Morbidity and mortality due to breast cancer
- Efficacy of interventions at reducing risk of breast cancer
- Cost effectiveness of interventions to identify or reduce risk of breast cancer

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
 Hand-searches of Published Literature (Secondary Sources)
 Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Searches for studies that included women with a family history of breast cancer, including BRCA1 and BRCA2 carriers were undertaken. However, in many instances studies relevant for family history were not found and therefore studies of general populations of women were also used.

Literature Search

Comprehensive searches were conducted in the major (11 in total) electronic bibliographic databases covering biomedical, nursing, psychological, social science, and health economic literature. The searches were conducted from March 2002 until February 2003. In addition, the Web sites of several Health Technology Assessment (HTA) and guideline producing bodies were consulted. Finally, the references lists of included articles were checked for additional references and citation searches were performed on key authors and papers in the Science and Social Science Citation Indexes.

Search Approach

A staged approach to searching was undertaken. This involved initially searching specifically for the search concepts of interest (e.g. tamoxifen, surgical interventions, etc.) in conjunction with familial breast cancer search terms. Where this yielded, few or no relevant references, the search was expanded to cover high level evidence (i.e. guidelines, systematic reviews, and randomised controlled trials) relating to breast cancer in general. Literature searches were also specifically undertaken in Medline, Embase, National Health Service (NHS) EED and Health Economic Evaluations Database (HEED), to specifically identify cost-effectiveness literature relating to familial breast cancer.

Search Restrictions

No date restrictions were applied to the searches, other than those imposed by the sources searched. Searches were, however, restricted to English language. No study or publication type restrictions were applied, with the exception of the more general breast cancer searches which were restricted to the highest levels of evidence (i.e., guidelines, systematic reviews, and randomised controlled trials). The corresponding methodological search filters used in Medline (Ovid) are given in Appendix 24 in the original guideline document.

Identification of Papers Related to Cost-Analysis

Guideline developers aimed to identify all relevant studies of cost-effectiveness across the entire scope of the guideline. A literature search was undertaken alongside the clinical literature review. Details of the databases searched and the filters used to identify relevant economic studies are given in Appendix 24 in the original guideline document. Titles and abstracts were then examined by hand in order to identify cost-effectiveness, cost-utility or cost-benefit studies (CEA, CUA, CBA). Members of the guideline development group provided additional references that had not been identified by the searches.

Studies that did not appear to be CEA, CUA, or CBA were not reviewed. This excluded a number of studies that examined only costs. Only primary studies

were included except in the area of mammographic surveillance since in this area there were no studies relevant directly to women with a familial history but a large number of studies relating to the cost-effectiveness of surveillance in other women. Consistent with the clinical review, the International Agency for Research on Cancer (IARC) screening report was used.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Evidence Categories

I a: Evidence from meta-analysis of randomised controlled trials

I b: Evidence from at least one randomised controlled trial

II a: Evidence from at least one controlled study without randomization

II b: Evidence from at least one other type of quasi-experimental study

III: Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies

IV: Evidence from expert committee reports or opinions and/or clinical experience of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Decision Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Synthesising the Evidence

Extraction tables and narrative descriptions of studies were used to provide the basis for conclusions about the findings of the body of evidence.

Many meta-analyses and systematic reviews included papers that involved populations of women with a family history and women without a family history, and in many instances did not differentiate in any given conclusions, etc. In the guideline if there were papers that were concerned primarily with women with a

family history, guideline developers often gave a précis of these studies in addition to the meta-analyses/systematic reviews, as this population is the one the guideline is primarily concerned with and may have information that is pertinent to this group but lost in the overall findings.

A decision analytic model was developed to assess the cost-effectiveness of genetic testing of women at varying degrees of breast cancer risk due to familial history. The model is discussed in Appendix 20 of the original guideline document.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus
Informal Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The derivation of recommendations usually involves assessment of evidence, processes of interpretation and consensus to arrive at recommendations. The mix of evidence, interpretation, and consensus will vary between topic areas. The grading of recommendations takes account of this and therefore variation may occur between different groups presented with the same evidence. Whilst evidence statements can be formulated without reference to the context in which clinicians practice, this is not always the case with recommendations.

The guideline development group used informal consensus methods to derive evidence statements and recommendations in areas where research literature was not available, drawing upon their clinical knowledge and experience. These are graded accordingly (D level recommendations).

There may be areas where the group was unable to reach consensus on an area, no matter whether evidence was available or not. Where this happened it was stated that a consensual recommendation could not be reached, the opposing views were presented and the final decision was left to the user of the guidelines.

Consensus was reached in all recommendations.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Recommendation Grades

Grade A - Directly based on category I evidence

Grade B - Directly based on category II evidence, or extrapolated recommendation from category I evidence

Grade C - Directly based on category III evidence, or extrapolated recommendation from category I or II evidence

Grade D - Directly based on category IV evidence, or extrapolated recommendation from category I, II or III evidence

COST ANALYSIS

Guideline developers reviewed cost-effectiveness, cost-utility or cost-benefit studies (CEA, CUA, CBA).

Cost-Effectiveness of Genetic Testing

It was difficult for guideline developers to draw definitive conclusions from the available studies. It appeared, however, that testing of women at "higher" risk is more cost-effective than women at moderate or average risk. However there is lack of data, including test costs and accurate costs for other interventions.

Base case results, shown in Table A in Appendix 20 of the original guideline document, show that genetic testing women at a very young age is dominated compared to a no testing alternative. The reason for this is that the model assumes that those women that undertake risk reducing surgery do so immediately. At a young age the risk of breast or ovarian cancer is relatively low compared to the reduction in quality of life suffered from risk reducing surgery. The benefits of risk reducing surgery are experienced to a greater extent in later years and are consequently not valued particularly highly due to discounting.

The base case results for testing at all other ages (except 65 years and over) indicate that health benefits are generated at a relatively low additional cost. The cost per quality adjusted life year (QALY) is relatively high (55k pounds sterling) for women aged 65 years. The reason for this is that whilst the costs of providing testing and surgery are immediate (financial and quality of life reduction for women), the benefits occur in later years (reduced incidence of disease). However, all cause mortality in older women is obviously higher and therefore the benefits accrued in future years are limited.

Cost-Effectiveness of Mammographic Cost Screening

Guideline developers reviewed an overview of published cost-effectiveness studies relating to mammographic screening in the general population from which two relevant issues are raised. Firstly, it is stated that screening of women below the age of 50 years is, in the general population, unlikely to be as cost-effective as increasing the frequency of screening for older women. Secondly the latter option is associated with substantially less uncertainty due to the unproven health benefits of screening younger women. The report states that, in relation specifically to screening high-risk women, this same uncertainty applies.

Cost-Effectiveness of Risk Reducing Surgery

Base cost-effectiveness results indicate that combination surgery is cost saving compared to surveillance. A series of one-way sensitivity analyses were performed and revealed that the results are particularly sensitive to the effectiveness of surgery in reducing cancer risks and the quality of life adjustments for relevant health states. The latter is particularly important given the small size of the sample used to derive QALY scores. Refer to the original guideline document regarding additional cost-effectiveness studies related to risk reducing surgery.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline was validated through two consultations.

1. The first draft of the guideline (The full guideline, NICE guideline and Quick Reference Guide) were consulted with Stakeholders and comments were considered by the Guideline Development Group (GDG).
2. The final consultation draft of the Full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments.

The final draft was submitted to the GRPs for review prior to publication.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Evidence categories (Ia-IV) and recommendation grades (A-D) are defined at the end of the "Major Recommendations" field.

Approaches to Care and Information Giving

D - Effective care involves a balanced partnership between patients and health care professionals. Patients should have the opportunity to make informed choices about any treatment and care and to share in decision making.

D - To ensure a patient-professional partnership, patients should be offered individually tailored information, including information about sources of support (including local and national organisations).

D - Tailoring of information should take into account format (including whether written or taped) as well as the actual content and form that should be provided (see Box 1 in Section 5.1 in the original guideline document).

D - Standard information should be evidence based wherever possible, and agreed at a national level if possible (the National Institute for Clinical Excellence's Information for the Public provides a good starting point).

D - Standard information should not contradict messages from other service providers, including commonly agreed information across localities.

Breast Awareness and Examination

D - Women at increased risk of breast cancer should be "breast aware" in line with Department of Health advice for all women (see www.cancerscreening.nhs.uk/breastscreen/breastaware.pdf).

Care of Women in Primary Care

Care and Management Approach - Primary Care

Family History Taking and Initial Assessment

D - When a woman presents with breast symptoms or has concerns about relatives with breast cancer, a first- and second-degree family history should be taken in primary care to assess risk, because this allows appropriate classification and care.

D - Health care professionals should respond to women who present with concerns, but should not, in most instances, actively seek to identify women with a family history of breast cancer.

D - In some circumstances it may also be clinically relevant to take a family history, for example for women older than age 35 years using an oral contraceptive pill or for women being considered for long-term hormone replacement therapy (HRT) use.

D - Women should be given the opportunity to discuss concerns about their family history of breast cancer if it is raised during a consultation.

D - A second-degree family history (that is, including aunts, uncles and grandparents) should be taken in primary care before explaining risks and options.

D - A second-degree family history needs to include paternal as well as maternal relatives.

D - Asking women to discuss their family history with relatives is useful in gathering the most accurate information.

C - Tools such as family history questionnaires and computer packages exist that can aid accurate collection of family history information and they should be made available.

D - For referral decisions attempts should be made to gather as accurate information as possible on:

- Age of diagnosis of any cancer in relatives
- Site of tumours
- Multiple cancers (including bilateral disease)
- Jewish ancestry

Primary Care Management

D - Women can be cared for in primary care if the family history shows only one first-degree or second-degree relative diagnosed with breast cancer at older than age 40 years, provided that none of the following are present in the family history:

- Bilateral breast cancer
- Male breast cancer
- Ovarian cancer
- Jewish ancestry
- Sarcoma in a relative younger than age 45 years of age
- Glioma or childhood adrenal cortical carcinomas
- Complicated patterns of multiple cancers at a young age
- Paternal history of breast cancer (two or more relatives on the father's side of the family).

D - Women who do not meet the criteria for referral should be cared for in primary care by giving standard written information (see Box 1 in Section 5.1 in the original guideline document).

Referral from Primary Care

D - Before a decision on referral is made, primary care professionals should note that a woman outside the 40-49 year age group who is estimated to be at moderate risk (for example, she has only one relative with breast cancer diagnosed at any age, or she has two relatives diagnosed with breast cancer older than an average age of 50 years) will not generally be offered additional mammography.

D - Women outside the 40–49 year age group may be referred for risk counselling and advice on risk management or consideration for prevention trials. Advice should be sought from the designated contact in secondary care about the appropriateness of referral.

D - Women who meet the following criteria should be offered referral to secondary care:

- One first-degree female relative diagnosed with breast cancer at younger than age 40 years, or
- One first-degree male relative diagnosed with breast cancer at any age, or
- One first-degree relative with bilateral breast cancer where the first primary was diagnosed at younger than age 50 years or
- Two first-degree relatives, or one first-degree AND one second-degree relative, diagnosed with breast cancer at any age, or
- One first-degree or second-degree relative diagnosed with breast cancer at any age AND one first-degree or second-degree relative diagnosed with ovarian cancer at any age (one of these should be a first-degree relative) or
- Three first-degree or second-degree relatives diagnosed with breast cancer at any age.

D - Advice should be sought from the designated secondary care contact if any of the following are present in the family history in addition to breast cancers in relatives not fulfilling the above criteria:

- Bilateral breast cancer
- Male breast cancer
- Ovarian cancer
- Jewish ancestry

- Sarcoma in a relative younger than age 45 years
- Glioma or childhood adrenal cortical carcinomas
- Complicated patterns of multiple cancers at a young age
- Paternal history of breast cancer (two or more relatives on the father's side of the family).

D - Discussion with the designated secondary care contact should take place if the primary care health professional is uncertain about the appropriateness of referral because the family history presented is unusual or difficult to make clear decisions about, or where the woman is not sufficiently reassured by the standard information provided.

D - Direct referral to a specialist genetics service should take place where a high risk predisposing gene mutation has been identified (for example, BRCA1, BRCA2, or TP53).

Information for Women Who Are Being Referred

C - Women who are being referred to secondary or tertiary care should be provided with written information about what happens at this stage (see Box 1 in Section 5.1 in the original guideline document).

Information and Ongoing Support for Women Who Are Not Being Referred

D - Support mechanisms (e.g., risk counselling, psychological counselling, and risk management advice) need to be identified and should be offered to women not eligible for referral and/or surveillance on the basis of age or risk level who have ongoing concerns.

Support for Primary Care

D - Support is needed for primary care health professionals to care for women with a family history of breast cancer. Essential requirements for support for primary care are:

- A single point and locally agreed mechanism of referral for women identified as being at increased risk
- Educational materials about familial breast cancer
- Decision-support systems
- Standardised patient information leaflets
- A designated secondary care contact to discuss management of "uncertain" cases.

Care of Women in Specialist (Secondary and Tertiary) Care

Specialist Care - Care and Management Approach

Care of Women in Secondary Care (Such as a Breast Care Team, Family History Clinic, or Breast Clinic Which Can Be Shared Between Trusts)

D - Care of women in secondary care (such as a breast care team, family history clinic, or breast clinic which can be shared between trusts) should be undertaken by a multidisciplinary team. It should include the following:

- Written protocols for management
- Central, standardised resources
- Mammographic surveillance available to National Health Service (NHS) Breast Screening programme standard
- Access to a team offering risk-reducing surgery
- Standardised written information
- Designated/lead clinicians
- A designated contact for primary care
- A designated contact in tertiary care
- Audit
- Clinical trials access
- Access to psychological assessment and counselling
- Information about support groups and voluntary organizations
- Administrative support

Family History Taking in Secondary Care

D - A family history should be taken when a woman presents with breast symptoms or has concerns about relatives with breast cancer.

D - A third degree family history should be taken in secondary care where possible and appropriate.

C - Tools such as family history questionnaires and computer packages exist that can aid accurate collection of family history information and risk assessment and they should be made available.

Management in Secondary Care

D - Women who meet the following criteria should be offered secondary care and do not require referral to tertiary care:

- One first-degree relative diagnosed with breast cancer at younger than age 40 years, or
- Two first-degree or second-degree relatives diagnosed with breast cancer at an average age of older than 50 years, or
- Three first-degree or second-degree relatives diagnosed with breast cancer at an average age of older than 60 years, or
- A formal risk assessment (usually carried out in tertiary care) or a family history pattern is likely to give risks of greater than 3-8% risk in the next 10 years for women aged 40 years, or a lifetime risk of 17% or greater but less than 30% provided that none of the following are present in the family history:
 - Bilateral breast cancer
 - Male breast cancer
 - Ovarian cancer
 - Jewish ancestry
 - Sarcoma in a relative younger than 45 years of age

- Glioma or childhood adrenal cortical carcinomas
- Complicated patterns of multiple cancers at a young age
- Very strong paternal history (four relatives diagnosed at younger than 60 years of age on the father's side of the family)

D - Women whose risk is less than that in the cases above can be referred back to primary care:

- With appropriate information being offered (see Box 1 in Section 5.1 in the original guideline document), and
- Support mechanisms (e.g., risk counseling, psychological counseling, and risk management advice) need to be identified and should be offered to women not eligible for referral and/or surveillance on the basis of age or risk level who have ongoing concerns.

Surveillance

D - Mammographic surveillance should not be available for women younger than age 30 years.

For women aged 30-39 years satisfying referral criteria for secondary or specialist care, mammographic surveillance should be carried out:

- D - Only as part of a research study (ethically approved) or nationally approved and audited service and
- Individualised strategies should be developed for exceptional cases, such as:
 - C - Women from families with BRCA1, BRCA2 or TP53 mutations
 - D - Women with equivalent high breast cancer risk

D - Support mechanisms (e.g., risk counselling, psychological counselling, and risk management advice) need to be identified and should be offered to women not being offered mammographic surveillance who have ongoing concerns.

C - All women satisfying referral criteria to secondary or specialist care (at moderate risk or greater) should be offered mammographic surveillance from age 40 years.

D - For women aged 40-49 years at moderate risk or greater, mammographic surveillance should be:

- Annual
- To National Health Service (NHS) Breast Screening Programme standards
- Audited
- Part of the NHS Research and Development Health Technology Assessment programme evaluation of mammographic surveillance of women younger than age 50 years with a family history wherever possible
- Only undertaken after provision of written information about the positive and negative aspects of surveillance

For women aged 50 years and older, surveillance should be:

- C - As part of the NHS Breast Screening Programme, screened every 3 years
- D - More frequent mammographic surveillance should take place only as part of a research study (ethically approved) or nationally approved and audited service.

and

- Individualised strategies should be developed for exceptional cases, such as:
 - C - Women from families with BRCA1, BRCA2 or TP53 mutations
 - D - Women with equivalent high breast cancer risk

D - If ongoing assessment of surveillance efficacy for women younger than age 50 years subsequently shows it is not cost effective, surveillance should be stopped.

Before decisions on surveillance are made, written patient information and discussion should be offered. This should:

- C - Reflect the possible reduced sensitivity of mammographic detection of the younger age group with dense breasts and the increased potential for further investigations
- Discuss the potential advantages and disadvantages of breast surveillance for early detection of breast cancer, including:
 - C - Radiation risks
 - D - The possible psychological impact of a recall visit

D - On the basis of current evidence, magnetic resonance imaging (MRI) and ultrasound should not be used in routine surveillance practice but may have a role in problem-solving mammographically detected abnormalities. (Note: several MRI studies have already been presented at major cancer meetings and will report in the next 2 years. This recommendation should be reviewed when they become available.)

Referral to Tertiary Care

D - Women who meet the following referral criteria should be offered a referral to tertiary care.

- At least the following female breast cancers only in the family:
 - Two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 50 years (at least one must be a first-degree relative), or
 - Three first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years (at least one must be a first-degree relative), or
 - Four relatives diagnosed with breast cancer at any age (at least one must be a first-degree relative)

or

- Families containing one relative with ovarian cancer at any age and, on the same side of the family:

- One first-degree relative (including the relative with ovarian cancer) or second-degree relative diagnosed with breast cancer at younger than age 50 years, or
- Two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years, or
- Another ovarian cancer at any age

or

- Families containing bilateral cancer (each breast cancer has the same count value as one relative):
 - One first-degree relative with cancer diagnosed in both breasts at younger than an average age of 50 years, or
 - One first-degree or second-degree relative diagnosed with bilateral breast cancer AND one first-degree or second-degree relative diagnosed with breast cancer at younger than an average age of 60 years.

or

- Families containing male breast cancer at any age with, on the same side of the family, at least:
 - One first-degree or second-degree relative diagnosed with breast cancer at younger than age 50 years, or
 - Two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years.

or

- A formal risk assessment has given risk estimates of:
 - A 20% or greater chance of a gene mutation being harboured in the family, or
 - A greater than 8% risk of developing breast cancer in the next 10 years, or
 - A 30% or greater lifetime risk of developing breast cancer

D - Clinicians should seek further advice from a specialist genetics service for families containing any of the following, in addition to breast cancers:

- Jewish ancestry
- Sarcoma in a relative younger than age 45 years of age
- Glioma or childhood adrenal cortical carcinomas
- Complicated patterns of multiple cancers at a young age
- Very strong paternal history (four relatives diagnosed at younger than 60 years of age on the father's side of the family)

D - The management of a high-risk woman may take place in secondary care if she does not want genetic testing or risk-reducing surgery and does not wish to be referred to a specialist genetics service.

D - Following initial consultation in secondary care, written information should be provided to reflect the outcomes of the consultation (see Box 1 in Section 5.1 in the original guideline document).

Care of Women in Tertiary Care

D - Care of women referred to tertiary care should be undertaken by a multidisciplinary team. In addition to having access to the components found in secondary care it should also include the following:

- Clinical genetic risk assessment
- Verification for abdominal malignancies and possible sarcomas

Family History Taking in Tertiary Care

D - A third-degree family history should be taken in tertiary care, if this has not been done previously.

D - For accurate risk estimation, the following are required:

- Age of death of affected and unaffected relatives
- Current age of unaffected relatives

D - In general, it is not necessary to validate breast cancer only histories (via medical records/cancer registry/death certificates).

D - If substantial management decisions such as risk-reducing surgery are being considered, and no mutation has been identified, clinicians should seek confirmation of breast cancer only histories (via medical records/cancer registry/death certificates).

D - Where no family history verification is possible, agreement by a multidisciplinary team should be sought before proceeding with risk reducing surgery.

D - Abdominal malignancies at young ages and possible sarcomas should be confirmed in specialist care.

Risk Assessment Tools

D - Computerized risk-assessment models can be helpful aids to risk assessment but can be misleading and should not yet totally replace careful clinical assessment of family trees with a manual approach.

Risk Communication in Tertiary Care

D - Women should be offered a personal risk estimate but information should also be given about the uncertainties of the estimation.

D - When a personal risk estimate is requested, it should be presented in more than one way (for example numerical value if calculated and qualitative risk).

D - Women should be sent a written summary of their consultation in specialist genetics clinics, which includes their personal risk information.

Risk-Reducing Surgery

D - In services offering risk-reducing surgery the following should be available:

- Facilities to verify family history and clinical genetic risk assessment
- Mammography before surgery
- Psychological assessment and counseling
- Information about support groups
- Onco/plastic skills.

D - If risk-reducing surgery is being considered, and no mutation has been identified, clinicians should seek confirmation of family history (via medical records/cancer registry/death certificates).

D - Where no family history verification is possible, agreement by a multidisciplinary team should be sought before proceeding with risk-reducing surgery.

Genetic Counselling (Tertiary Care)

C - Women meeting criteria for referral to tertiary care should be offered a referral for genetic counselling regarding their risks and options.

D - Women attending genetic counselling should receive standardised information beforehand describing the process of genetic counselling, information to obtain prior to the counselling session, the range of topics to be covered, and brief educational material about hereditary breast cancer and genetic testing.

C - Predictive genetic testing should not be offered without adequate genetic counselling.

Genetic Testing (Tertiary Care)

D - All high-risk women should have access to information on genetic tests aimed at mutation finding.

D - Pre-test counselling (preferably two sessions) should be undertaken.

D - Discussion of genetic testing (predictive and mutation finding) should be undertaken by a health professional with appropriate training.

D - High-risk women and their affected relatives should be informed about the likely informativeness of the test (the meaning of a positive and a negative test) and the likely timescale of being given the results.

Mutation Tests

D - Tests aimed at mutation finding should first be carried out on an affected family member, where possible.

D - Women from families with a 20% or greater chance of carrying a mutation such as BRCA1, BRCA2, or TP53 should have access to testing.

D - The development of a genetic test for a family should usually start with the testing of an affected individual (mutation searching/screening) to try to identify a mutation in the appropriate gene (such as BRCA1, BRCA2, or TP53).

D - A search/screen for a mutation in a gene (such as BRCA1, BRCA2, or TP53) should aim for as close to 100% sensitivity as possible for detecting coding alterations and the whole gene(s) should be searched.

Risk Reducing Mastectomy (Tertiary Care)

D - Bilateral risk-reducing mastectomy is appropriate only for a small proportion of women who are from high-risk families and should be managed by a multidisciplinary team.

D - Bilateral mastectomy should be raised as a risk-reducing strategy option with all women at high risk.

D - Women considering bilateral risk-reducing mastectomy should have genetic counselling in a specialist cancer genetics clinic before a decision is made.

D - Discussion of individual breast cancer risk and its potential reduction by surgery should take place and take into account individual risk factors, including the woman's current age (especially at extremes of age ranges).

D - Family history should be verified where no mutation has been identified before bilateral risk-reducing mastectomy.

D - Where no family history verification is possible, agreement by a multidisciplinary team should be sought before proceeding with bilateral risk-reducing mastectomy.

D - Pre-operative counselling about psychosocial and sexual consequences of bilateral risk-reducing mastectomy should be undertaken.

D - The possibility of breast cancer being diagnosed histologically following a bilateral risk-reducing mastectomy should be discussed pre-operatively.

D - All women considering bilateral risk-reducing mastectomy should be able to discuss their breast reconstruction options (immediate and delayed) with a member of a surgical team with specialist oncoplastic or breast reconstructive skills.

D - A surgical team with specialist oncoplastic/breast reconstructive skills should carry out risk reducing mastectomy and/or reconstruction.

D - Women considering bilateral risk-reducing mastectomy should be offered access to support groups and/or women who have undergone the procedure.

Risk Reducing Oophorectomy

D - Risk-reducing bilateral oophorectomy is appropriate only for a small proportion of women who are from high-risk families and should be managed by a multidisciplinary team.

D - Information about bilateral oophorectomy as a potential risk-reducing strategy should be made available to women who are classified as high risk.

D - Family history should be verified where no mutation has been identified before risk-reducing bilateral oophorectomy.

D - Where no family history verification is possible, agreement by a multidisciplinary team should be sought before proceeding with risk-reducing bilateral oophorectomy.

D - Any discussion of bilateral oophorectomy as a risk-reducing strategy should take fully into account factors such as anxiety levels on the part of the woman concerned.

D - Health care professionals should be aware that women being offered risk-reducing bilateral oophorectomy may not have been aware of their risks of ovarian cancer as well as breast cancer and should be able to discuss this.

D - The effects of early menopause should be discussed with any woman considering risk-reducing bilateral oophorectomy.

D - Options for management of early menopause should be discussed with any woman considering risk-reducing bilateral oophorectomy, including the advantages, disadvantages, and risk impact of HRT.

D - Women considering risk-reducing bilateral oophorectomy should have access to support groups and/or women who have undergone the procedure.

D - Women considering risk-reducing bilateral oophorectomy should be informed of possible psychosocial and sexual consequences of the procedure and have the opportunity to discuss these issues.

D - Women not at high risk who raise the possibility of risk-reducing bilateral oophorectomy should be offered appropriate information and, if seriously considering this option, should be offered referral to the team that deals with women at high risk.

D - Women undergoing bilateral risk-reducing oophorectomy should have their fallopian tubes removed as well.

Risk Factors

D - Women should be provided with standardised written information about risk, including age as a risk factor (see Box 1 in Section 5.1 in the original guideline document).

D - Modifiable risk factors should be discussed on an individual basis with each woman in the relevant care setting.

Hormone Replacement Therapy

C - Women with a family history of breast cancer who are considering taking, or are already taking, HRT should be informed of the increase in breast cancer risk with type and duration of HRT.

D - Advice to individual women should vary according to the individual clinical circumstances (such as asymptomatic, age, severity of menopausal symptoms, or osteoporosis).

D - HRT usage in a woman at familial risk should be restricted to as short a duration and as low a dose as possible. Oestrogen-only HRT should be prescribed where possible.

D - A woman having an early (natural or artificial) menopause should be informed of the risks and benefits of HRT, but generally HRT usage should be confined to women younger than age 50 years if at moderate or high risk.

D - Alternatives to HRT should be considered for specific symptoms such as osteoporosis or menopausal symptoms.

D - Consideration should be given to the type of HRT if it is being considered for use in conjunction with risk-reducing gynaecological surgery.

Hormonal Contraceptives

C - Advice to women up to age 35 years with a family history of breast cancer should be in keeping with general health advice on the use of the oral contraceptive pill.

C - Women aged over 35 years with a family history of breast cancer should be informed of an increased risk of breast cancer associated with taking the oral contraceptive pill, given that their absolute risk increases with age.

C - For women with BRCA1 mutations, the conflicting effects of a potential increased risk of breast cancer under the age of 40 years and the lifetime protection against ovarian cancer risk from taking the oral contraceptive pill should be discussed.

D - Women should not be prescribed the oral contraceptive pill purely for prevention of cancer, although in some situations reduction in ovarian cancer risk may outweigh any increase in risk of breast cancer.

D - If a woman has a BRCA1 mutation and is considering a risk-reducing oophorectomy before the age of 40 years, the oral contraceptive pill should not be prescribed purely for the reduction in ovarian cancer risk.

Breastfeeding

C - Women should be advised to breast feed if possible because this is likely to reduce their risk of breast cancer, and is in accordance with general health advice.

Alcohol consumption

C - Women with a family history should be informed that alcohol may increase their risk of breast cancer slightly. However, this should be considered in conjunction with any potential benefit of moderate alcohol intake on other conditions (such as heart disease) and adverse effects associated with excessive alcohol intake.

Smoking

D - Women should be advised not to smoke, in line with current health advice.

Weight and Physical Activity

C - Women should be advised on the probable increased postmenopausal risk of breast cancer from being overweight.

C - Women should be advised about the potential benefits of physical exercise on breast cancer risk.

Menstrual/Reproductive Factors

D - Health care professionals should be able to provide information on the effects of hormonal and reproductive factors on breast cancer risk.

Definitions:

Evidence Categories

I a: Evidence from meta-analysis of randomised controlled trials

I b: Evidence from at least one randomised controlled trial

II a: Evidence from at least one controlled study without randomization

II b: Evidence from at least one other type of quasi-experimental study

III: Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies

IV: Evidence from expert committee reports or opinions and/or clinical experience of respected authorities

Recommendation Grades

Grade A - Directly based on category I evidence

Grade B - Directly based on category II evidence, or extrapolated recommendation from category I evidence

Grade C - Directly based on category III evidence, or extrapolated recommendation from category I or II evidence

Grade D - Directly based on category IV evidence, or extrapolated recommendation from category I, II or III evidence

CLINICAL ALGORITHM(S)

Algorithms are provided in the original guideline document for primary care management, secondary care management, and tertiary care management.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence is stated for each recommendation (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

The guideline is intended to help health care providers appropriately classify and care for women at risk of familial breast cancer. The intention of the guideline is that:

- Women at or near population risk of developing breast cancer are cared for in primary care.
- Women at moderate risk of developing breast cancer are generally cared for in secondary care.
- Women at high risk of developing breast cancer are cared for in tertiary care.

POTENTIAL HARMS

- For some women, however, risk reducing mastectomy was associated with adverse psychosocial effects: 36% in one study reported diminished or greatly diminished satisfaction with their body appearance; and adverse effects were reported in terms of emotional stability (9%), stress (14%), self-esteem (18%), sexual relationships (23%) and feelings of femininity (25%).

- Postoperative complications were reported in a minority of women in one of the observational studies, and in a review of hospital records in Canada, 14% of women who underwent risk reducing oophorectomy experienced adverse effects from the surgery.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Guidelines are only one type of information that health care professionals may use when making decisions about patient care. It is assumed that this guideline, like all guidelines, will be used by health care professionals who will also bring to bear their clinical knowledge and judgement in making decisions about caring for individual patients. It may not always be appropriate to apply either specific recommendations or the general messages in this document to each individual or in every circumstance. The availability of resources may also influence decisions about patient care, including the adoption of recommendations.
- This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Health professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of health professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Local health communities should review their existing practice for the management of women at risk of familial breast cancer against this guideline. The review should consider the resources required to implement the recommendations set out in the original guideline document, the people and the processes involved, and the timeline over which full implementation is envisaged. It is in the interests of women at risk of familial breast cancer that the implementation timeline is as rapid as possible.

Information on the cost impact of this guideline in England is available on the National Institute for Clinical Excellence (NICE) website and includes a template that local communities can use (www.nice.org.uk/CG014costtemplate).

The implementation of this guideline will build on the National Cancer Plan (Department of Health, 2000), and the National Health Service (NHS) plan in Wales, Improving Health in Wales.

Suggested audit criteria are listed in Appendix D in the National Institute for Clinical Excellence (NICE) version of the original guideline document. These can be used as the basis for clinical local audit, at the discretion of those in practice.

The following have been identified as key priorities for implementation:

Approaches to Care

1. Effective care involves a balanced partnership between patients and healthcare professionals. Patients should have the opportunity to make informed choices about any treatment and care and to share in decision making.
2. To ensure a patient-professional partnership, patients should be offered individually tailored information, including information about sources of support (including local and national organisations).
3. Standard written information regarding familial risk and breast cancer risk factors should be developed for use in primary, secondary, and tertiary care, to provide consistent advice to women.

Family History and Referral

4. When a woman presents with breast symptoms or has concerns about relatives with breast cancer, a first- and second-degree family history should be taken in primary care to assess risk, because this allows appropriate classification and care.
5. Healthcare professionals should respond to women who present with concerns, but should not, in most instances, actively seek to identify women with a family history of breast cancer.
6. Local protocols for the care of women at risk of familial breast cancer should be developed with clear referral mechanisms between primary, secondary and tertiary care, and with appropriate facilities.

Care

7. Access to psychological support and assessment is a key part of the package of care needed for many women covered by this guideline.
8. All women aged 40-49 years satisfying referral criteria to secondary or specialist care (at moderate risk or greater) should be offered annual mammographic surveillance.
9. Mammographic surveillance should only be undertaken after provision of information about its potential advantages and disadvantages for the early detection of breast cancer, and where offered, this should be of high quality (equivalent to National Health Service Breast Screening Programme standard) and audited.
10. Genetic testing is appropriate only for a small proportion of women who are from high-risk families.
11. Risk-reducing surgery (mastectomy and/or oophorectomy) is appropriate only for a small proportion of women who are from high-risk families and should be managed by a multidisciplinary team.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators

Chart Documentation/Checklists/Forms

Clinical Algorithm

Patient Resources
Quick Reference Guides/Physician Guides

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Primary Care. Clinical guidelines for the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care. London (UK): National Institute for Clinical Excellence (NICE); 2004 May. 311 p. [309 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 May

GUIDELINE DEVELOPER(S)

National Collaborating Centre for Primary Care - National Government Agency
[Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Guideline Development Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Professor Gareth Evans (Chair), Consultant Clinical Geneticist, St Mary's Hospital, Manchester; Nasim Bahar, Patient Representative; Dr Michelle Barclay, Patient Representative, Policy Manager, Breakthrough Breast Cancer; Professor Doug Easton, Professor of Genetic Epidemiology, University of Cambridge, Strangeways Research Laboratory; Dr Jon Emery, Cancer Research UK Clinician Scientist, General Practice Research Unit, University of Cambridge; Dr Jonathan Gray, Consultant in Medical Genetics & Clinical Director, Medical Genetics Service in Wales; Dr Jane Halpin, Public Health, Watford & Three Rivers PCT, St. Albans; Dr Penny Hopwood, Consultant Psychiatrist and Psycho-Oncologist, Christie Hospital NHS Trust, Manchester; Aileen McIntosh, Deputy Director, Sheffield Evidence Based Guidelines Programme, Public Health, SchARR, University of Sheffield; Dr James Mackay, Consultant Genetic Oncologist, The Genetics Unit, Institute of Child Health, London; Carmel Sheppard, Consultant Nurse Breast Care, Portsmouth Hospitals NHS, Trust/University of Southampton; Mr Mark Sibbering, Consultant Breast Surgeon, Derby City General Hospital, Derby; Wendy Watson, Patient Representative, Hereditary Breast Cancer Helpline; Dr Allan Wailoo, Health Economist, Sheffield Health Economics Group, SchARR, University of Sheffield; Professor Valerie Beral, Director, Department of Health Breast Screening Advisory Committee, also Cancer Research UK Epidemiology Unit, University of Oxford (resigned February 2003); Clare Shaw, Research Associate, Public Health, SchARR, University of Sheffield (until May 2003)

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Clinical Excellence \(NICE\) Web site](#).

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. 11 Strand, London, WC2N 5HR.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- National Collaborating Centre for Primary Care. Familial breast cancer. The classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care. NICE guideline London (UK): National Institute for Clinical Excellence (NICE); 2004 May. 40 p. (Clinical guideline; no. 14). Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Clinical Excellence \(NICE\) Web site](#).
- Familial breast cancer. The classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care. Quick reference guide.

- London: National Institute for Clinical Excellence. 2004 May. 12 p. Available in Portable Document Format (PDF) from the [NICE Web site](#).
- Costing clinical guidelines: familial breast cancer. London: National Institute for Clinical Excellence. 2004 May. 24 p. Available in Portable Document Format (PDF) from the [NICE Web site](#).
 - Cost template: familial breast cancer. London: National Institute for Clinical Excellence. 2004 May. 24 p. Available in Portable Document Format (PDF) from the [NICE Web site](#).

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N0561. 11 Strand, London, WC2N 5HR.

Additionally, Audit Criteria can be found in Chapter 9 of the [original guideline document](#).

PATIENT RESOURCES

The following is available:

- Women with breast cancer in the family: Understanding NICE guidance - information for women at risk of familial breast cancer, their families and the public. London: National Institute for Clinical Excellence. 2004 May. 46 p. Available in Portable Document Format (PDF) from the [National Institute for Clinical Excellence \(NICE\) Web site](#).

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N0562. 11 Strand, London, WC2N 5HR.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on January 24, 2005. The information was verified by the guideline developer on March 17, 2005.

COPYRIGHT STATEMENT

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at <http://www.guideline.gov/about/inclusion.aspx>.

NGC, AHRQ, and its contractor ECRI make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

© 1998-2006 National Guideline Clearinghouse

Date Modified: 10/2/2006

